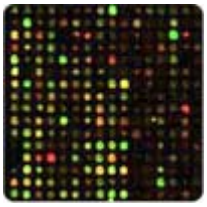
Basic Information

Background



The mission of the U.S. Environmental Protection Agency is to safeguard public health and the environment from harmful effects that may be caused by exposure to pollutants in the air, water, soil, and food. Protecting human health and the environment carries with it the challenge of assessing the risk that is posed by tens of thousands of chemicals. The large number of chemicals that the Agency must evaluate and the many different legal statutes that regulate chemicals have traditionally made it impossible for the Agency to evaluate every chemical with the most rigorous testing strategies. Instead, standard toxicity tests have been limited to only a small number of chemicals. Today, however, the young field of computational biology offers the possibility that, with advances in computational biology's subdisciplines (e.g., genomics, proteomics, and metabonomics), scientists may have the ability to develop a more detailed understanding of the risks posed by a much larger number of chemicals. The application of the tools of computational biology to assess the risk chemicals pose to human health and the environment is termed *Computational Toxicology*. Within this website, Computational Toxicology is defined as the application of mathematical and computer models to predict adverse effects and to better understand the mechanism(s) through which a given chemical induces harm.

Three strategic objectives of the computational toxicology initiative are to:

1. improve understanding of the linkages in the continuum between the source of a chemical in the environment and adverse outcomes;
2. provide predictive models for screening and testing; and
3. improve quantitative risk assessment.

View a flow chart outlining the Source-to-Outcome Continuum. This Continuum describes the process on how a specific environmental release can eventually cause an adverse outcome in a specific source.

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Computational Disciplines

Computational toxicology includes several disciplines including:

- Computational chemistry, which refers to physical-chemical mathematical modeling at the molecular level and includes such topics as quantum chemistry, force fields, molecular mechanics, molecular simulations, molecular modeling, molecular design, and cheminformatics;
- Computational biology or bioinformatics, which refers to development of molecular biology databases and the analysis of the data; and
- Systems biology, which refers to the application of mathematical modeling and reasoning to the understanding of biological systems and the explanation of biological phenomena.

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"Omic" Disciplines

The development of "omic" technologies has evolved into three scientific disciplines:

- genomics which is defined as the study of genes and their function,
- proteomics which is defined as the study of the full set of proteins encoded by a genome, and
- metabonomics which is defined as the study of the total metabolite pool.

Several recent technological advances now make it possible to develop molecular profiles using genomic, proteomic, and metabolomic methods in order to identify the effects that chemicals may have on living

organisms or the environment. Although the technology continues to change and improve, conducting these types of analyses is no longer a question of capability. The use of "omic" technology to study toxicological questions is called toxicogenomics. Return to top

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Guidance on Use of Genomics Data

EPA's Interim Genomics Policy issued on June 25, 2002, outlines the current state of the application of genomics data which includes genomics, transcriptomics, and proteomics. The interim guidance is available at: http://epa.gov/osa/spc/genomics.htm

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Computational Toxicology Implementation Steering Committee

The Computational Toxicology Implementation Steering Committee (CTISC) was formed in January 2004 with the specific charge of implementing the recently developed Framework for Computational Toxicology Research Program.

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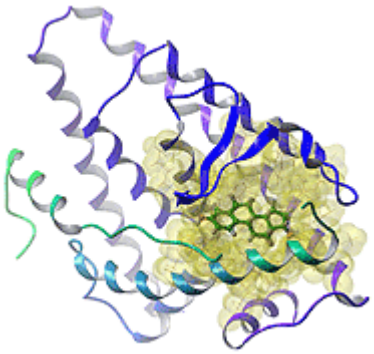
Finding a Better Way



EPA has actively pursued collaborations and partnerships with other research groups having capabilities in computational toxicology. For example, EPA has a Memorandum of Understanding with CIIT and held workshops with the Department of Energy laboratories to pursue potential collaborative projects. Discussions are also underway with the Joint Genomic Institute to sequence the genome of test species used by the Agency for risk assessment. Discussions have been held with the National Center for Toxicogenomics at the National Institute of Environmental Sciences concerning contributions to their Chemical Effects in Biological Systems knowledge base.

To enhance the research program, a group has been formed comprised of scientists dedicated to the coordination and facilitation of genomic, proteomic, and bioinformatic sciences. In addition, development is underway of bioinformatic tools such as the Distributed Structure-Searchable Toxicity (DSSTox) database network. This network is a community-wide effort to promote and encourage the use of standard format, chemical structure inclusive files (structure data files or SDF) for storing, sharing, and disseminating public chemical toxicity data. The larger goal of DSSTox is to facilitate widespread and open access to public toxicity data and structure searchability and comparability across toxicity databases.

The overall goal of the computational research effort at ORD is to develop the use of computational approaches to provide EPA with better tools for quantitative risk assessment and more efficient strategies for prioritizing chemicals for screening and testing. Through the computational toxicology initiative, EPA will strengthen its foundation for making sound scientific decisions. Return to top

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Impact of High Performance Computing

Parallel to efforts in computational biology have been major advances in computational speed and access to data. Less than a decade ago, describing the complexity of chemical behavior in biological systems was severely limited because realistic models presented combinatorial and other problems beyond the capabilities of most computers. In the field of bioinformatics, for example, major advances were made not from faster statistical analysis of data after the acquisition, but from the integration of computational and data acquisition technologies. It is now possible to consider how to evaluate the vast amounts of information generated by "omic" technologies using data-mining tools made possible by rapid advances in computational storage capacity and speed. Return to top

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